Clinical Update

Naval Postgraduate Dental School
National Naval Dental Center
Bethesda, Maryland

Vol. 22, No. 9 September 2000

Vesiculobullous diseases affecting the oral cavity: pemphigus

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Dermatologic diseases frequently present with concomitant lesions involving the oral cavity and therefore become an important part of any dental practice. Skin and oral mucosa are both subjected to a significant amount of environmental stress and as such, are uniquely designed to withstand these challenges. This is accomplished on a microscopic level with adhesion molecules that anchor keratinocytes, the cells of the superficial epithelial layer, to one another and to the underlying basement membrane (1). These molecules are attacked by a person's own antibodies in vesiculobullous diseases of the skin and oral mucosa. Diseases of this kind are divided into two major categories: pemphigus and pemphigoid, which are distinguished by an intraepithelial or subepithelial splitting of the epithelium respectively. An understanding of these two diseases can provide a rational diagnostic and therapeutic approach to patient diagnosis and treatment (2). Detection and treatment of blistering disorders that manifest early in the oral cavity may prevent widespread skin involvement.

The condition known as pemphigus represents four related chronic autoimmune vesiculobullous diseases: pemphigus vulgaris, pemphigus vegetans, pemphigus erythematosus, and pemphigus foliaceus. Pemphigus, which is a rare disease varying in incidence from 0.5-3.2 cases per 100,000 population per year, is characterized by intraepithelial vesicles and bullae of the skin and oral mucosa (3). Although most commonly a disease of middle age, it has been reported to occur in children and older adults with men and women equally affected. Pemphigus has been reported in all races and ethnic groups with a significantly increased prevalence observed in the Jewish population and those of Mediterranean descent (4). Pemphigus vulgaris, (vulgaris, Latin meaning common), is the most frequently diagnosed of these diseases and if left untreated, can result in the patient's death (5). In approximately 50% to 70% of patients with pemphigus vulgaris, the disease originates in the oral cavity, which gives the dentist the opportunity for an early and potentially life saving diagnosis (6).

Patients usually complain of oral soreness with examination showing superficial, ragged erosions and ulcerations on the oral mucosa. The bullae are fragile and break easily, leaving denuded areas that extend easily with pressure (7). Fluid filled vesicles can occasionally be seen on mucosal surfaces but usually are not present long enough to biopsy. A positive Nikolsky sign (a bulla that can be induced on normal mucosa when firm lateral pressure is exerted) characterizes pemphigus vulgaris. Erosive lesions may involve the entire oral cavity, but they are most commonly seen on the ventral tongue, palate, buccal mucosa, and gingival mucosa (5). More than 90% of patients with pemphigus vulgaris will have oral lesions at some time during the course of their disease (8). These lesions may persist for long periods of time before expanding to other sites. The extraoral manifestation of pemphigus vulgaris is a flaccid blister that arises on normal or erythematous skin and typically involves the scalp, face and axillae.

Diagnosis of pemphigus is based on clinical presentation and confirmed by histologic and direct immunofluorescence studies. When sampling tissue for pathologic interpretation, it is important to submit clinically normal tissue adjacent to the blister or ulcer. This allows interpretation of both the epithelium and the transition between the lesion and neighboring tissue. After harvesting, the specimen should then be split, placing one of the halves in 10% formalin and the remaining tissue in Michel's solution. Prior planning

to acquire the proper fixatives is paramount to obtaining the correct diagnosis for your patient.

Being a tissue specific autoimmune disease of skin and mucosa, pemphigus is caused by antibodies acting against the cell surface of keratinocytes causing disruption of cell-to-cell adhesion. Microscopically, pemphigus vulgaris displays an intraepithelial separation just above the basal cell layer. Intercellular edema within the epithelial layers leads to separation between the keratinocytes leading to subsequent blister formation. The basal epidermal cells remain attached to the basement membrane but become detached from one another in a pattern thought to resemble a row of tombstones (8). The free-floating, rounded, acantholytic cells found within the vesicle can be detected by a Tzank preparation wherein the base of a blister is scraped and examined microscopically for acantholytic cells (9). The diagnosis of pemphigus vulgaris should be confirmed by direct immunofluorescence performed on fresh tissue submitted in Michel's solution (5). This test shows a consistent deposition of immunoglobulins (IgG) and a variable deposition of complement (C3) on the epithelial cell surfaces without deposition along the basement membrane zone.

Prompt treatment is vital to decrease the potential lethality of untreated pemphigus, and is directed at lowering the production of the autoantibodies. Systemic corticosteroids, usually prednisone, alone or in conjunction with other immuno-suppressive drugs like azathioprine, can accomplish this effect (2). Unfortunately, long term-high dose corticosteroid therapy is associated with numerous side effects such as hyperglycemia, hypertension, osteoporosis, gastrointestinal bleeding and psychotic reactions (9). Periodontal therapy is also an essential component in the treatment of pemphigus as the gingival involvement may represent an exaggerated response to bacterial plaque (9).

Pemphigus rarely undergoes complete remission and the mortality rate is in the range of 5-10% even with attentive medical management. Common causes of death are infection and pulmonary embolism, both considered a side effect of the immuno-suppressive effect of the medications. Staphylococcus aureus is the most frequent bacterial pathogen, with skin being the primary site of infection (5). Referral to a physician is indicated, and good communication between the dentist, physician, and patient is essential to good treatment and follow up.

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